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     (FILE 'MEDLINE, CANCERLIT, BIOTECHDS, EMBASE, CAPLUS, BIOSIS' ENTERED AT
     11:29:35 ON 17 MAR 2003)
                 DEL HIS
L1          39240 S MICROPARTICLE OR MICROSPHERE
L2         306151 S EMULSI?
L3         106208 S EVAPORAT?
L4            587 S L3 AND L2 AND L1
L5           2425 S PEG AND DEXTRAN
L6              3 S L5 AND L4
L7              1 DUP REM L6 (2 DUPLICATES REMOVED)
L8         740447 S DISPERS? OR DISCONTINUOUS
L9             95 S L8 AND L4
L10            72 S L9 AND PHASE
L11            37 DUP REM L10 (35 DUPLICATES REMOVED)
L12       3101431 S DNA OR NUCLEIC OR PLASMID
L13            15 S L12 AND L4
L14             9 DUP REM L13 (6 DUPLICATES REMOVED)
L15            11 S L5 AND L3
L16             5 DUP REM L15 (6 DUPLICATES REMOVED)
L17             1 S PEG AND L2 AND L1 AND L12 AND AQUEOUS
L18           491 S PEG AND L1
L19            92 S L18 AND L8
L20             5 S L19 AND L12
L21             5 DUP REM L20 (0 DUPLICATES REMOVED)

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L7 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
AN 97402448 MEDLINE
DN 97402448 PubMed ID: 9259512
TI Biodegradable polymeric microparticles for drug delivery and vaccine formulation: the surface attachment of hydrophilic species using the concept of poly(ethylene glycol) anchoring segments.
AU Coombes A G; Tasker S; Lindblad M; Holmgren J; Hoste K; Toncheva V; Schacht E; Davies M C; Illum L; Davis S S
CS Department of Pharmaceutical Sciences, University of Nottingham, University Park, UK.
SO BIOMATERIALS, (1997 Sep) 18 (17) 1153-61.
Journal code: 8100316. ISSN: 0142-9612.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199712
ED Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971202
AB Poly(ethylene glycol)-**dextran** (**PEG**-DEX) conjugates have been used as a combined stabilizer and surface modifier to produce resorbable poly(DL-lactide-co-glycolide) (PLG) microparticles by an **emulsification**/solvent **evaporation** technique. The use of **PEG** or **dextran** polymers alone was incapable of producing microparticles. Particle size measurements revealed smaller mean particle sizes (480 nm) and improved polydispersity when using a 1.2% **PEG** substituted conjugate relative to a 9% substituted material (680 nm). PLG microparticles modified by post-adsorbed **PEG**-DEX conjugates flocculated in 0.01 M salt solutions, whereas PLG microparticles prepared using **PEG**-DEX as a surfactant were stable in at least 0.5 M NaCl solutions. Surface modification of PLG microparticles was confirmed by zeta potential measurements and surface analysis using X-ray photoelectron spectroscopy. The presence of surface exposed **dextran** was confirmed by an immunological detection method using a **dextran** -specific antiserum in an enzyme-linked immunosorbent assay. The findings support a model in which the **PEG** component of the **PEG** -DEX conjugate provides an anchor to the **microparticle** surface while the **dextran** component extends from the particle surface to contribute a steric stabilization function. This approach offers opportunities for attaching hydrophilic species such as targeting moieties to biodegradable microparticles to improve the interaction of drug carriers and vaccines with specific tissue sites.

L11 ANSWER 28 OF 37 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN 96339585 EMBASE

DN 1996339585

TI Development of furosemide loaded polymethylmethacrylate microspheres.

AU Sa B.; Ghosh A.

CS Dept. of Pharmaceutical Technology, Jadavpur University,Calcutta - 700 032, India

SO Indian Drugs, (1996) 33/10 (521-524).
ISSN: 0019-462X CODEN: INDRBA

CY India

DT Journal; Article

FS 037 Drug Literature Index

LA English

SL English

AB Furosemide-loaded polymethylmethacrylate microparticles were prepared by **emulsion**-solvent **evaporation** technique using aqueous **phase** as **dispersion** medium to minimize the use of hazardous organic solvents. Among the different **emulsion** stabilizers, methylcellulose and hydroxy propylcellulose, in a concentration range of 0.0025 to 0.1% w/v were found suitable for the formation of discrete and spherical microparticles. The spherical shape of tne microparticles was not influenced by variation in concentration of either methylcellulose or hydroxy propylcellulose. Actual drug content in the microparticles was almost equal to theoretical drug load and was not influenced significantly by change in either methylcellulose or hydroxy-propylcellulose concentrations.

L14 ANSWER 8 OF 9 MEDLINE DUPLICATE 4

AN 1999093470 MEDLINE

DN 99093470 PubMed ID: 9874713

TI PLGA microspheres containing **plasmid DNA**: preservation of supercoiled **DNA** via cryopreparation and carbohydrate stabilization.

AU Ando S; Putnam D; Pack D W; Langer R

CS Massachusetts Institute of Technology, E25-342, 45 Carleton Street, Cambridge, Massachusetts 02139, USA.

SO JOURNAL OF PHARMACEUTICAL SCIENCES, (1999 Jan) 88 (1) 126-30.
Journal code: 2985195R. ISSN: 0022-3549.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199903

ED Entered STN: 19990402
Last Updated on STN: 19990402
Entered Medline: 19990322

AB Biodegradable microspheres containing **plasmid DNA** have potential uses as mediators of transfection in cells, particularly phagocytic cells such as macrophages. However, the hydrophilic nature and the structural instability of supercoiled **DNA** preclude its facile encapsulation in polymer matrixes such as poly(d, l-lactic-co-glycolic acid) (PLGA) by traditional methods. We initially studied the microencapsulation of **plasmid DNA** using the established water-in-oil-in-water double-**emulsion** solvent-**evaporation** method and found that (1) the encapsulation efficiency was low (about 20%), (2) the microencapsulation procedure nicked (degraded) the supercoiled **DNA**, and (3) lyophilization of the **microsphere** also nicked the **DNA**. We have therefore designed a new **microsphere** preparation method (called cryopreparation) to specifically address these concerns. Using the cryopreparation method, the aqueous phase of the primary **emulsion** containing the **plasmid DNA** is frozen and then subjected to homogenization. Because there is no shear stress inside a solid, we hypothesized that freezing the aqueous phase of the primary **emulsion** would help to preserve the supercoiled **plasmid DNA** during formation of the secondary **emulsion**. We also hypothesized that the formation of crystals from buffers within the primary **emulsion** was a causative factor for nicking during freezing or lyophilization, and that disruption of the crystal formation by the addition of saccharides into the primary **emulsion** would improve the supercoiled-**DNA** content of the spheres. Our results support the two hypotheses. Not only was the supercoiled-**DNA** content increased from 39% to over 85%, but the encapsulation efficiency was also elevated from 23% to over 85%.

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L14  ANSWER 5 OF 9  CAPLUS  COPYRIGHT 2003 ACS
AN   2001:380725  CAPLUS
DN   135:2561
TI   Continuous-flow method for preparing microparticles
IN   Hedley, Mary Lynne; Hsu, Yung-Yueh; Tyo, Michael
PA   Zycos, Inc., USA
SO   PCT Int. Appl., 47 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
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PI   WO 2001036583       A1   20010525      WO 2000-US31770  20001117
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             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
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             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1230338          A1   20020814      EP 2000-978814   20001117
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 1999-443654      A1   19991119
     WO 2000-US31770     W    20001117
```

AB The invention is based on the discovery of a method for scalable, continuous flow prodn. of a **nucleic** acid-contg. **microparticle** that maintains the structural integrity of the assocd. **nucleic** acid and results in a **microparticle** having a purity suitable for introduction into an animal (e.g., human) host. Microparticles prepd. according to the continuous flow processes described herein can be used for delivery of a **nucleic** acid for gene therapy, antisense therapy, vaccination, treatment of autoimmune disease, and either specific or non-specific modulation of an immune response (e.g., via cytokine regulation). The microparticles can addnl. be used to deliver **nucleic** acid encoding a protein or peptide useful in any type of therapy.

RE.CNT 3   THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

L21 ANSWER 5 OF 5 CAPLUS

AN 1995:546956 CAPLUS

DN 122:274119

TI Hydrophobic polymeric pharmaceutical microparticles

IN Andrianov, Alexander K.; Langer, Robert S.

PA Virus Research Institute, USA; Massachusetts Institute of Technology

SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9508320	A1	19950330	WO 1994-US10692	19940921
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN				
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	US 5500161	A	19960319	US 1993-124816	19930921
	CA 2172040	AA	19950330	CA 1994-2172040	19940921
	AU 9478001	A1	19950410	AU 1994-78001	19940921
	EP 720471	A1	19960710	EP 1994-928640	19940921
	EP 720471	B1	20010418		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AT 200616	E	20010515	AT 1994-928640	19940921
	ES 2159305	T3	20011001	ES 1994-928640	19940921
PRAI	US 1993-124816	A	19930921		
	WO 1994-US10692	W	19940921		

AB A method for the prepn. of microparticles, and the product thereof, that include **dispersing** a substantially water insol. non-ionic or ionic polymer in an aq. soln. in which the substance to be delivered is also dissolved, **dispersed** or suspended, and then coagulating the polymer together with the substance by impact forces to form a **microparticle**. In an alternative embodiment, the **microparticle** is formed by coagulation of an aq. polymeric **dispersion** through the use of electrolytes, pH changes, org. solvents in low concns. (the minimal amt. necessary to break up the **dispersion**), or temp. changes to form polymer matrixes encapsulating biol. materials. Thus 60 mg of fluorescein-labeled bovine serum albumin was dissolved in 3 mL of 30% aq. soln. **dispersion** of Eudragite NE 30D and then spraying the aq. **dispersion** in a flask contg. 200 mL of deionized water using Turbotack air-atomizing nozzle. The flow rate of the polymeric **dispersion** was 150.mu.L/min, the air pressure was 25 psi, and the distance between the nozzle and surface of water was 30 cm. The resulting microparticles were spherical with an av. diam. of 1-10 .mu.m and encapsulation efficiency of 65%.

malonate) microparticles with encapsulated paclitaxel were prepd.

L21 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 2002:654974 CAPLUS
DN 137:190745
TI Emulsion-based processes for making microparticles
IN Gibson, John W.; Holl, Richard J.; Tipton, Arthur J.
PA Southern Biosystems, Inc., USA
SO U.S., 16 pp., Cont.-in-part of U. S. 6,291,013.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6440493	B1	20020827	US 2000-726108	20001129
	US 2002142093	A1	20021003		
	US 6291013	B1	20010918	US 1999-303842	19990503
	WO 2000066087	A2	20001109	WO 2000-US11781	20000502

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-303842 A2 19990503
WO 2000-US11781 A2 20000502

AB Processes for making microparticles, preferably contg. an active agent, are provided. In a preferred embodiment, the process involves prepg. (1) a **dispersed** phase contg. an agent in a soln. of polymer and a first solvent; (2) a continuous phase contg. a surfactant, and a second solvent that is totally or partially immiscible with the first solvent; and (3) an extn. phase that is a nonsolvent for the polymer, a solvent for the continuous phase components, and a solvent for the first solvent, wherein the first solvent has soly. in the extn. phase of between about 0.1% and 25% by wt. Then, the **dispersed** phase and the continuous phase are mixed to form an emulsion, and the emulsion is then briefly mixed with a suitable quantity of extn. phase to induce skin formation at the interface of the **dispersed** and continuous phases. Remaining solvent is removed by an evapn. process step. The emulsification and solvent removal steps are preferably conducted in a continuous process. The brief extn. step prior to evapn. minimizes the loss of active agent from the microparticles, and reduces the required vol. of extn. phase as compared to other extn.-based processes. Alternate emulsification methods and solvent removal methods, such as incremental extn., cryogenic extn., or membrane sepn., also are provided, and can be used in various combinations to make microparticles. Fluorescein-loaded microspheres were prepd. using polylactide.

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L20	L18 same l1	12	L20
L19	L18 with l4	2	L19
L18	l17 with l2	354	L18
L17	emulsif$	176389	L17
L16	l2 with l3	1	L16
L15	l8 and l5	1	L15
L14	l8 same l4	0	L14
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L12	l8 with l5	0	L12
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L10	l8 with l3	0	L10
L9	l8 with l3L8	0	L9
L8	l1 with l2	35	L8
L7	l1 with l2 with l3 with l5	0	L7
L6	dextran	39963	L6
L5	evaporat?	61571	L5
L4	peg	70026	L4
L3	emulsif?	7308	L3
L2	microparticle	15154	L2
L1	dispersed phase	10292	L1

END OF SEARCH HISTORY